

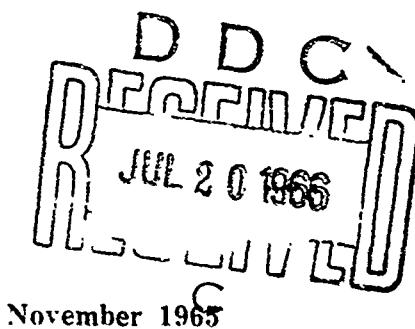
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AD 635378

## MONKEY COLONY MANAGEMENT

ROBERT J. YOUNG, D.V.M.

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## Monkey Colony Management

Robert J. Young, D.V.M.

THE DISCIPLINE of laboratory animal medicine encompasses disease control, nutrition, genetics, breeding, housing, environment, and administration. Since World War II, the research animal has gained an increasingly important role in all research endeavor. This has created a need for refinements in colony husbandry; emphasis has been placed on control of all extrinsic factors which affect results, plus the development of skills and techniques designed to deliver a "processed animal" free of disease, and standardized as to diet, weight, age, conformation, genetics, and other requirements.

### Procurement of Animals and Supplies

The successful animal colony manager is in reality a link between the producer or animal importer and the research worker. His responsibilities begin even before the animal enters the quarantine area of the laboratory. It behoves him to make at least one inspection of the vendor's premises, to assure himself that the animals to be procured are from healthy stock, maintained under proper conditions of husbandry, and are free of disease. He must also assure himself of the reliability of the vendor from a professional and fiscal standpoint. He has the additional responsibility of determining that animals are being shipped under proper conditions. Animals in transit should be provided ample space, food, and water at regular intervals, and protection against rough handling and wide variations in temperature. They should be picked up promptly at destination.

Equally as important as the procurement of the animal itself is the procurement of proper materials to support and care for the

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animal once he has arrived at the laboratory. The supplies include drugs, protective clothing for animal attendants, sterilization equipment, food, house-cleaning equipment, litter, and other material necessary to maintain the health of large numbers of animals.

### Quarantine

The properly maintained quarantine area provides a buffer between the valuable research animals in the laboratory and pathogens which may be seeking to invade from the outside, using the recently purchased animals as hosts. The quarantine period is utilized to isolate and possibly destroy those pathogens which constitute a threat to the health of the other animals; to treat those animals with clinical signs of disease; and to rid animals of parasites, fungi, and other potential health hazards.

### Utilization of Personnel and Equipment

The proper assignment and training of personnel can constitute almost a full-time job in itself. All personalities must be understood by the animal colony supervisor and the proper assignment made to utilize particular talents or to compensate for shortcomings. In addition, the successful colony supervisor must be constantly alert for better and more efficient methods. He should scrutinize every operation with a critical eye, keeping in mind such questions as:

Can this be accomplished more economically?

Are the personnel involved being utilized to their full capabilities?

Can the work be organized so as to provide greater economy of operation?

What will be the results of this decision on the over-all experimental program?

Last, and most important, the supervisor should seek the advice of those who are ac-

tually doing the work. This not only gleans many helpful ideas but also elicits greater support and enthusiasm for the accomplishment of the task.

#### **Construction and Housekeeping Chores**

The key to economical and efficient operation lies in a well-planned, well-constructed building. Cages must be designed to facilitate cleaning, catching, and handling. The water and feeding systems must be designed for economy of operation and should be automatic to effect a savings in manpower. Construction material must be noncorrosive and durable to withstand rough handling during washing operations and assault by large animals. Floors should be impervious and constructed with the proper slope to facilitate drainage and cleaning. The walls, to a height of at least 6 ft., should be tiled or covered with other impervious material which will not harbor roaches or other vermin, and which are capable of withstanding steam sterilization. Drains in the floors should be countersunk, and should have a catch basin for large debris. The drain pipes themselves should be large enough to preclude clogging at critical times during the wash-down period. Good heat and temperature control is necessary for valuable research animals, especially since at times these animals are undergoing stress and their defense mechanisms are temporarily or permanently destroyed. Sanitary waste disposal must be planned, with incineration of all diseased tissue as well as droppings from rooms containing animals with infectious organisms. The colony manager should be an important member of the planning committee for any construction being contemplated.

#### **Sanitation Program**

The key to the maintenance of any colony is the establishment of sound hygienic principles. The life cycles of disease organisms and parasites must be disrupted.

We at the Radiobiological Laboratory of the University of Texas and the United States Air Force are of the opinion that we

substantially decreased the in-colony disease incidence by the institution of a combination plan of chemical disinfection plus steam sterilization. Each cage in the colony was steamed at least every 10 days and was chemically disinfected 5 days a week. It is especially important that animals which have been isolated, or even those with loose feces at repeated intervals, be placed on an accelerated sterilization regimen to prevent spread of disease to adjacent animals. One of the more difficult aspects of this is the prevention of the spread of disease organisms through fomites, such as contaminated housecoats, gloves, and shoes.

This was controlled by frequent laundering of outer garments and use of ultraviolet light to sterilize the leather gloves worn by handlers. Ultraviolet sterilization was provided by means of a plywood box in which a light was mounted and a series of pegs on which the gloves were suspended. These pegs were staggered in such a way that the light could reach the major portion of the surface of the gloves. In addition, footbaths were provided at strategic locations, especially in the quarantine area and in the isolation area. These footbaths contained solutions with a phenol coefficient of 3%.

#### **Housing**

The rhesus monkey is extremely nervous and energetic and is difficult to house. Animals involved in experiments should definitely be housed in individual cages. The main colony at our radiobiological facility was housed indoors. Animal rooms were approximately 27 by 18 ft. with 9-ft. ceilings. The floors were concrete; the walls were either concrete blocks or glazed tile. The space was adequate to house 4 racks, each of which held 10 individual cages. These units had an over-all length of 11 ft. and a height of 78 inches. Cages contained in each unit measured 2 by 2 by 2 ft. A larger cage is recommended for animals over 15 lb. These cages were constructed of corrosion-resistant aluminum 6061 alloy. Punched aluminum panels, welded and riveted construction, and a large, swinging front door are factors

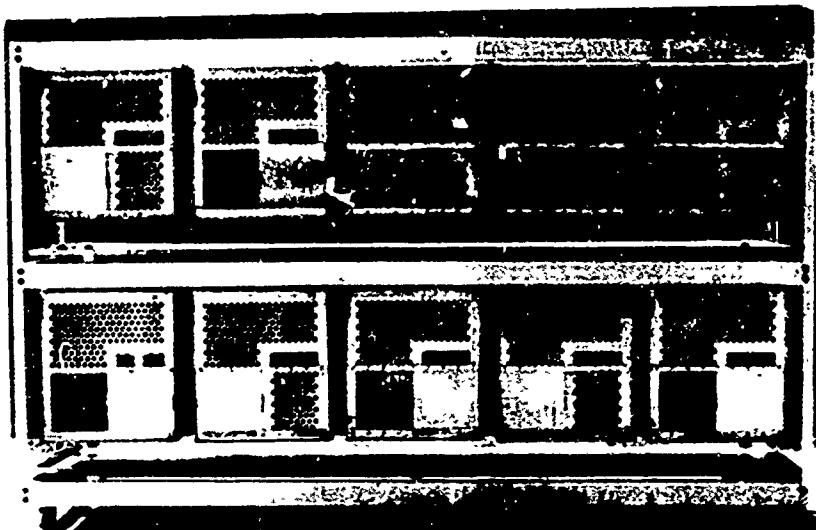


Fig. 1—Ten-unit aluminum cage.

which facilitated cleaning the cage thoroughly. Within the large hinged door was a small sliding door for removing the animal (Fig. 1).

Another type cage which comes in these sizes is the so-called "turkey-type" cage (Fig. 2), which has the advantages of allowing better visibility, providing a squeeze-type apparatus useful in restraint, and housing more animals per room. It must be provided with dividers, however, to prevent contact of adjacent animals and disease transmission.

Water was supplied by means of a pipe running behind each cage. A pneumatic quick-release coupling attaches the supply

to the cage outlet. This allows the cage to be removed from the rack without disturbing the water system. The water was turned on twice daily for 10 minutes. Pans under the cage catch excess water and drain it away.

#### Animal Records

Since many research animals must be kept for months, and even years, the establishment of an adequate record system is imperative. The record system must be tailored to satisfy many specifications. The information it contains must be readily accessible and must be designed to supply

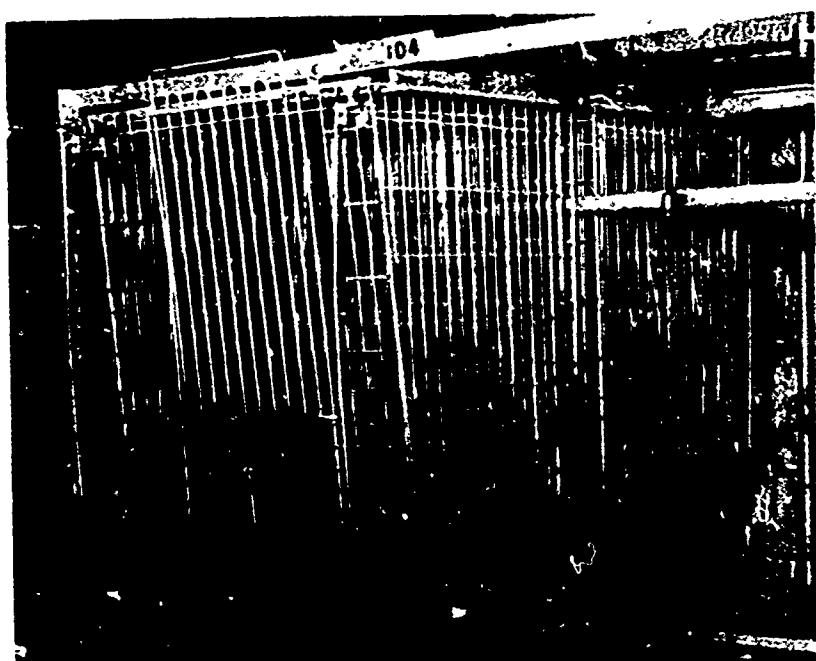


Fig. 2—"Turkey-type" cage in rock suitable for housing 16 primates.

information on a multitude of subjects, such as the age and purchase weight of the animal, the vendor's name, date of purchase, date of issue to investigator, contract number, and name and phase number of the experiment to which the animal is assigned. Disease incidence, diagnostic information, and chemotherapy used to combat disease must be coded in such a way that the information it contains can be secured on any particular disease should it be needed at a later date. It must contain accession number and cause of death. Information regarding immunization, tuberculosis-testing results, and location of all animals in the colony must be included. Our experience at this Radiobiological Laboratory indicated that key sort cards were satisfactory.

A continuous inventory system must be conducted to assure that the proper supply of needed drugs, animal food, and equipment for maintenance of the colony is available, and that the proper purchase orders are accomplished to maintain inventory levels.

*Weight Records.*—Weight records must be obtained for all animals in the colony to pinpoint any wide fluctuations in weight, and to provide information on individual animals for assignment to research projects for use when anesthetics are indicated, and for the establishment of drug dosage levels when treatment is indicated. Monthly weight records were kept on a chart for each animal. This aided in administering drugs, especially anesthetics. Weights of monkeys in common age groups were averaged and plotted on a chart to show monthly gains and losses. A downward trend often allows closer scrutiny to the husbandry program in time to avert colony-wide disease.

#### Diet

Few animals respond so quickly to their diet as the monkey; consequently, an adequate diet is of paramount importance. To insure the desired ration, a guaranteed-analysis feed was used (Table 1). The meal was fortified with a commercial vitamin preparation and mixed with water in a large

TABLE 1—Sample Diet for a 6- to 1<sup>1</sup>/2 lb. Rhesus Monkey

1/3 lb.	Commercial primate meal	Monday - Friday
1	Orange	Tuesday
1	Apple	Thursday
20	Dry biscuits	Saturday and Sunday

electric food mixer. It was then formed into 1/2-lb. squares by a "patty" machine. With each 50 lb. of meal, 4 oz. of a vitamin preparation\* and 5 Gm. of ascorbic acid were mixed.

This diet was prepared fresh each day. Animals were fed once daily. Isonicotinic acid hydrazide,\*\* 5 mg./kg. of body weight, was added to the mixture as an aid in the prevention of tuberculosis.

#### Restraint

Since many animals in the colony were in longevity studies and maintained for many years, they attained great strength, and some weighed as much as 25 to 30 lb. This, of course, created a problem of restraint. The beginner may find the restraint of small animals facilitated by the use of carrying cages or restraining chairs. With increasing familiarity, these smaller animals can usually be controlled by one person. As they become older and larger, they are difficult to handle. Monkeys over 3 years of age develop large canine teeth which make them more aggressive and, consequently, more dangerous and difficult to restrain. The general policy was to remove these canine teeth whenever possible without jeopardizing health. Two well-trained handlers can usually control one of these animals.

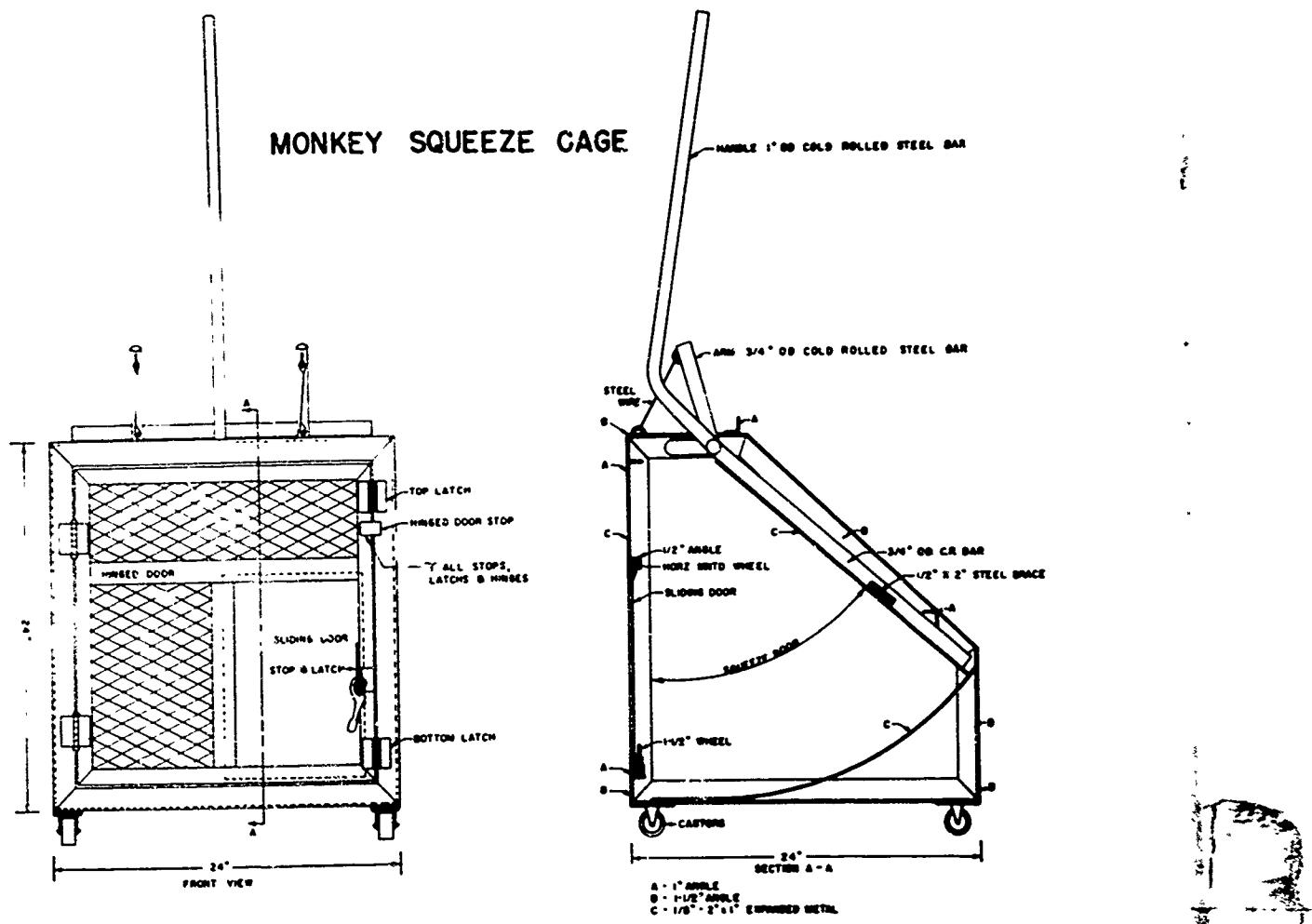
Personnel handling monkeys should wear double leather gloves with leather arm-guards to protect them against biting and scratching. Using this method of protection, the handler puts his hand in the cage, daring the monkey to attack. When he grasps the animal by one arm and lifts him from the cage, backward pressure is placed on both arms to control the animal. With the exception of very vicious animals, this pro-

\*ViDaylin, Abbott Laboratories, North Chicago, Ill.  
\*\*Isoniazid, Eli Lilly and Co., Indianapolis, Ind.

Fig. 3—Monkey carrying cage.



Fig. 4—Monkey squeeze cage.



cedure is easy for the handler and causes minimal stress to the animal.

A carrying cage was frequently used for moving animals (Fig. 3). This cage is small, approximately a 1-ft. cube, with a sliding door on one end. After minimal training, the monkey will learn to run into the carrying cage when it is placed against its "home" cage. With this method, the monkey is not handled manually; this allows for faster handling and less trauma.

For the larger, more difficult-to-handle monkey, the squeeze cage (Fig. 4) is used. The monkey is forced against a sliding door, and the appendages are made available for parenteral injections. The sliding door also provides a means of removing the animal from the squeeze cage. The use of nets to restrain the monkey is a safe procedure but is a slow, cumbersome process.

It was often desired to provide an animal in a semianesthetized condition to facilitate procedures such as ophthalmic examination, tuberculosis testing larger monkeys, minor surgical practices, and weighing. For these procedures, the tranquilizing drugs were employed. The monkey responds to tranquilizers in a uniform manner and tolerates these drugs well. Oral preparations may be added to the food ball with satisfactory results.

Parenteral administration is usually preferred. Chlorpromazine\* may be administered intramuscularly at the rate of 0.65 mg./lb. of body weight and reaches maximum drug effect in 1 to 2 hours. The intravenous route requires half this dose and becomes effective immediately.

Optimal doses for barbiturates were determined (Tables 2 and 3). Fast-acting injectables require a minimal number of technical assistants and equipment for administration. Inhalant anesthetics are well tolerated but are used only when their certain advantages are specifically indicated.

Synthetic opiates are occasionally indicated and have been utilized with highly satisfactory results. An average dose of meperidine hydrochloride\*\* is 12 mg., re-

peated as indicated. This dosage is usually adequate for the 8- to 20-lb. monkey.

#### **Preventive Medicine**

Our preventive medicine program involves rigid conformance to several rules:

- 1) Animals must pass 3 negative tuberculin tests during a 90-day quarantine period.
- 2) Only necessary personnel are permitted in the animal quarters.
- 3) Animal handlers must wash hands and equipment between handling groups of monkeys.
- 4) Aseptic surgery is practiced in minor as well as major operations.
- 5) A visual health appraisal is made of each caged animal both mornings and evenings. Loose feces are collected and examined for evidence of parasites and pathogenic bacteria.
- 6) Every animal is weighed each month. Feeding problems, parasitic infections, and other colony problems can often be detected from the comparative body weights.
- 7) Cages, dropping trays, and rooms are washed daily, and floors are mopped with 3% lysol solution.
- 8) Cages are steam-cleaned monthly, and carrying cages are cleaned and disinfected in a 3% lysol solution after each use.
- 9) Animals suspected of being diseased are housed in isolation.

#### **Quarantine Procedure**

The first quarantine procedure for all monkeys purchased for the colony began at the vendor's residence. Prior to inspecting the animals they were given intrapalpebral injections of 0.1 ml. USDA tuberculin. The eyes were then examined at 24, 48, and 72 hours for a reaction. All reactors were killed. Animals were also examined for external parasites and for overt clinical signs of intestinal or respiratory disease. Selected animals were then transported via air to the laboratory.

At the laboratory, the monkeys were confined to quarantine for a minimum of 90 days; during this period they had to pass 3

\*Thorazine, Smith, Kline and French, Philadelphia, Pa.

\*\*Demerol, Winthrop Laboratories, New York, N.Y.

TABLE 2—Pentothal Sodium Dosage Chart for Rhesus Monkeys (50 mg./ml., i.v.)

Animal weight (lb.)	(kg.)	Dosage level (mg./lb.)				
		8	9	10	11	12
1.0	0.45	0.16 ml.	0.18 ml.	0.20 ml.	0.22 ml.	0.24 ml.
2.0	0.91	0.32	0.36	0.40	0.44	0.48
3.0	1.36	0.48	0.54	0.60	0.66	0.72
4.0	1.82	0.64	0.72	0.80	0.88	0.96
5.0	2.27	0.80	0.90	1.00	1.10	1.20
6.0	2.73	0.96	1.08	1.20	1.32	1.44
7.0	3.18	1.12	1.26	1.40	1.54	1.68
8.0	3.64	1.28	1.44	1.60	1.76	1.92
9.0	4.09	1.44	1.62	1.80	1.98	2.16
10.0	4.55	1.60	1.80	2.00	2.20	2.40
11.0	5.00	1.76	1.98	2.20	2.42	2.64
12.0	5.45	1.96	2.16	2.40	2.64	2.88
13.0	5.91	2.08	2.34	2.60	2.86	3.12
14.0	6.36	2.24	2.52	2.80	3.08	3.36
15.0	6.82	2.40	2.70	3.00	3.30	3.60
16.0	7.27	2.56	2.88	3.20	3.52	3.84
17.0	7.73	2.76	3.06	3.40	3.74	4.08
18.0	8.18	2.88	3.24	3.60	3.96	4.32
19.0	8.64	3.04	3.42	3.80	4.18	4.56
20.0	9.09	3.20	3.60	4.00	4.40	4.80
21.0	9.55	3.36	3.78	4.20	4.62	5.04
22.0	10.00	3.52	3.96	4.40	4.84	5.28
23.0	10.45	3.68	4.14	4.60	5.06	5.52
24.0	10.91	3.84	4.32	4.80	5.28	5.76
25.0	11.36	4.00	4.50	5.00	5.50	6.00

TABLE 3—Pentobarbital Sodium Dosage Chart for Rhesus Monkeys (60 mg./ml., i.v.)

Animal weight (lb.)	(kg.)	Dosage level (mg./lb.)				
		9	10	11	12	13
1.0	0.45	0.15 ml.	0.17 ml.	0.18 ml.	0.20 ml.	0.22 ml.
2.0	0.91	0.30	0.33	0.37	0.40	0.43
3.0	1.36	0.45	0.50	0.55	0.60	0.65
4.0	1.82	0.60	0.68	0.73	0.80	0.87
5.0	2.27	0.75	0.83	0.92	1.00	1.08
6.0	2.73	0.90	1.00	1.10	1.20	1.30
7.0	3.18	1.05	1.16	1.28	1.40	1.52
8.0	3.64	1.20	1.33	1.46	1.60	1.73
9.0	4.09	1.35	1.50	1.65	1.80	1.95
10.0	4.55	1.50	1.66	1.83	2.00	2.17
11.0	5.00	1.65	1.83	2.01	2.20	2.38
12.0	5.45	1.80	2.00	2.20	2.40	2.60
13.0	5.91	1.95	2.16	2.38	2.60	2.82
14.0	6.36	2.10	2.32	2.56	2.80	3.03
15.0	6.82	2.25	2.50	2.75	3.00	3.25
16.0	7.27	2.40	2.66	2.93	3.20	3.47
17.0	7.73	2.55	2.82	3.11	3.40	3.68
18.0	8.18	2.70	2.99	3.30	3.60	3.90
19.0	8.64	2.85	3.15	3.48	3.80	4.12
20.0	9.09	3.00	3.32	3.66	4.00	4.34
21.0	9.55	3.15	3.49	3.85	4.20	4.55
22.0	10.00	3.30	3.65	4.03	4.40	4.78
23.0	10.45	3.45	3.82	4.21	4.60	5.00
24.0	10.91	3.60	4.00	4.40	4.80	5.20
25.0	11.36	3.75	4.16	4.58	5.00	5.42



Fig. 5—Restraint apparatus and cassette holder with monkey in position for radiograph.

more negative tuberculin tests, administered at 30-day intervals.

All animals were examined radiographically for pneumonic or tubercular lesions. The detection of tuberculosis by this means is a difficult procedure because simian tuberculosis is a widely disseminated disease, and in the primate there is almost total absence of calcification and fibrotic resolution, making radiographic diagnosis extremely difficult.

A special restraint apparatus (Fig. 5) fa-

cilitated radiographic examination of animals in the quarantine colony. With this apparatus, we found it unnecessary to expose any of the animal attendant personnel during radiography. An additional advantage is that the viscera is in a normal position. By monitoring the animal, the radiograph can be made while the animal is inhaling, thereby assuring maximal inflation of the lungs. Initially, only an anteroposterior radiograph is taken. If any questionable lesions are found, a lateral radiograph is then taken.

The turkey-type cages in the quarantine area enable us to provide individual therapy to isolated animals. The usual procedure, however, is to medicate the entire quarantine colony by mixing the medications in the feed.

Although few instances have been recognized in which a colony disease was directly attributable to human carriers, visitors are not permitted to visit the quarantine area.

#### Isolation of Diseased Animals

An isolation area which would accommodate approximately 1% of the animals was adequate. Animals in the main colony suspected of having a disease which might be communicable to other animals were immediately isolated, and diagnostic procedures were instituted.

#### Breeding Colony

Breeding rhesus monkeys in captivity presents problems that are much more complicated than those presented by merely maintaining monkeys in captivity. Housing, caging, nutrition, and care of monkeys being held for research do present numerous problems, but these are far simpler than the problem of providing environmental conditions under which consistent reproduction will occur. First, and most essential, requirement for the environmental conditions under which animals must be maintained if reproduction is to take place is that all the normal needs, both physiologic and psychologic, of the animal be provided. Basically, it may be stated that maximal

reproduction occurs when all the environmental conditions combine to permit the animal to adjust.

**Caging.**—Caging presents a difficult problem of which the most fundamental condition is size. The cages used at the Radiobiological Laboratory were small chimpanzee cages which measured 3.0 by 3.5 by 5.0 ft., with a shelter box attached to the back, the dimensions of which are 2.0 by 2.5 by 2.5 ft. (Fig. 6).

**Breeding Period.**—The rhesus monkey in captivity does not appear to have a seasonal breeding period. They ovulate in summer as well as through the winter. In the *Macaca mulatta*, with a 28-day cycle, there are only 2 days in the middle of the cycle in which ovulation occurs. There are usually 2 or 3 cycles necessary before impregnation, then a 5-month pregnancy. At the end of the pregnancy, the ovary is inactive and suppressed; ovulation is not resumed for 2 or 3 months. One young a year is about the best reproductive rate that can be expected. There is an occasional sterile animal and an occasional animal that is asocial.

Menarche bleeding usually occurs between 1½ to 2½ years; the average being approximately 722 days, just under 2 years.

Testicular development in the monkey is comparable to that of man, 3 years in the monkey being considered roughly equivalent to 15 years in man.

Our experience indicates that for all practical purposes, *M. mulatta* is not suitable for breeding younger than 4 years.

**Optimum Mating Time for Pregnancy in the Monkey.**—Evidence indicates that ovulation occurs during mid-menstruation, from the 9th through the 18th day. Peak days for ovulation appear to be days 11, 12, 13, and 14. All timing is related to the first day of the preceding menses. The females were removed from living quarters and placed in a cage with an adult male. Analysis of all 48-hour mating which resulted in pregnancy disclosed that the 24-hour period common to the greatest number of matings extends from noon of the 11th day to that of the 12th day.

#### Research

The competent supervisor is constantly engaged in basic research on all aspects of animal care. He must be engaged in fundamental research dealing with disease, nutrition, physiology, psychology, and genetics.

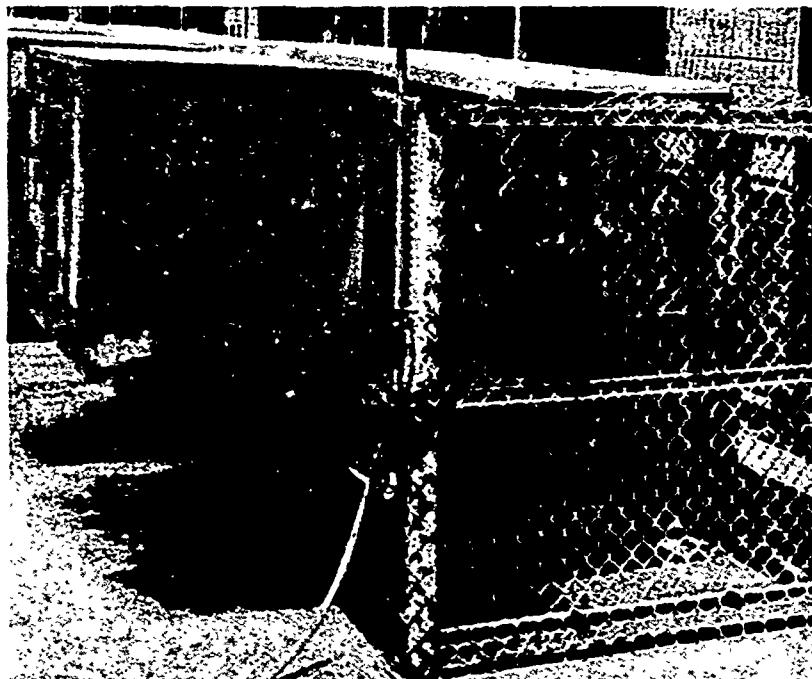


Fig. 6—Wire cage with attached shelter box used in the primate breeding colony.

In addition to the fundamental research, a great deal of applied research needs to be done. Such subjects as optimum cage size, sanitation procedures, temperature, lighting, and humidity badly need carefully controlled study. In addition, time permitting, the supervisor can serve as a valuable member of the research team, lending support in the areas of surgery, physiology, virology, and bacteriology, and in a number of other areas.

The commonly occurring primate diseases, their diagnosis and treatment, have been adequately covered in published reports.<sup>1-3</sup>

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Unclassified

Security Classification

**DOCUMENT CONTROL DATA - R&D**

(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)

1 ORIGINATING ACTIVITY (Corporate author) <b>USAF School of Aerospace Medicine Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas</b>	2a REPORT SECURITY CLASSIFICATION <b>Unclassified</b>
	2b GROUP

3 REPORT TITLE

**MONKEY COLONY MANAGEMENT**

4 DESCRIPTIVE NOTES (Type of report and inclusive dates)

5 AUTHOR(S) (Last name, first name, initial)

**Young, Robert J.**

6 REPORT DATE <b>November 1965</b>	7a TOTAL NO. OF PAGES <b>10</b>	7b. NO. OF REFS <b>3</b>
8a CONTRACT OR GRANT NO.	8a. ORIGINATOR'S REPORT NUMBER(S)	
b PROJECT NO.	<b>SAM TR 66-214</b>	
c.	9b. OTHER REPORT NO(S) (Any other numbers that may be assigned this report)	

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11 SUPPLEMENTARY NOTES <b>Reprinted from the J. Amer. Vet. Med. Ass. 147(10): 1053-1062 (1965)</b>	12. SPONSORING MILITARY ACTIVITY <b>USAF School of Aerospace Medicine Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas</b>
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13 ABSTRACT

The discipline of laboratory animal medicine encompasses disease control, nutrition, genetics, breeding, housing, environment, and administration. Supplies needed by the laboratory include drugs, protective clothing for animal attendants, sterilization equipment, food, house-cleaning equipment, litter, and other material necessary to maintain the health of large numbers of animals. The quarantine period is utilized to isolate and possibly destroy those pathogens which constitute a threat to the health of the other animals. Material for cages must be non-corrosive and durable to withstand rough handling during washing operations and assault by large animals. In-colony disease incidence can be decreased by the institution of combinations plan of chemical disinfection plus steam sterilization. Establishment of an adequate record system is imperative.

**UNCLASSIFIED**

Security Classification

14 KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Monkey Colony Management						
Disease control, monkeys						
Cages, rhesus monkeys						
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